## REMARKS

Claims 1-13 remain pending in the present application. Claims 14-41 are canceled. The amendment to claims 1 and 13 regarding local administration at the surgical site finds basis at page 6, lines 4-5 and at page 11, lines 5-7, as well as throughout the specification as a whole. No new matter is added.

## Rejections under 35 U.S.C. §112

Claims 1-13 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite. Applicants believe the rejections to have been mooted in view of their amendment herein, as suggested by the Examiner in the outstanding Office Action at page 3, last line. Withdrawal of the rejections is respectfully requested.

## Rejection under 35 U.S.C. §101 for Double Patenting

Claims 1-13 stand provisionally rejected under 35 U.S.C. §101 for statutory double patenting over claims 1-13 of co-pending application no. 10/797,367. Applicants note a corresponding rejection in the co-pending application regarding claims 14-41. The accompanying amendment cancels non-elected claims 14-41 in the present application, which should remove the statutory double patenting rejection in the co-pending application, and will likewise cancel claims 1-13 of that application upon their next response, so as to remove the present rejection in this application.

## Rejection under 35 U.S.C. 102/103 over Adachi et al.

Claims 1-5 and 7-13 are rejected under 35 U.S.C. §102(b) as anticipated by, or alternatively under 35 U.S.C. §103(a) as obvious over Adachi et al.

Applicants traverse these bases for rejection and respectfully request reconsideration and withdrawal thereof.

Adachi et al. is discussed at length in the present specification at page 5, lines 6-26 (identified as "Shinya et al."), wherein Applicants indicate that the authors administered Tranilast orally both pre- and post-operatively in a rat intraperitoneal adhesion model.

***Lack of Anticipation***

Adachi et al. fail to disclose or suggest "...locally administering a composition comprising a delivery vehicle containing Tranilast, or an analog thereof, directly onto said tissue surfaces at the surgical site..." as is required by claim 1. Accordingly, Adachi et al. cannot be deemed to anticipate the presently claimed invention of claims 1-13, for lack of identity of subject matter. Withdrawal of the rejection is requested on this basis.

***Lack of Obviousness***

For the same reasons as stated above, Applicants submit that Adachi et al. is insufficient to establish a *prima facie* case of obviousness as to the present claims, i.e. Adachi et al. fail to disclose or suggest each and every claim limitation.

Withdrawal of the rejection is requested on this basis.

**Rejection under 35 U.S.C. 103 over Adachi et al.**
**In view of Hanson**

Claims 1-13 are rejected under 35 U.S.C. §103(a) as obvious over Adachi et al. in view of Hanson. Applicants traverse this basis for rejection and respectfully request reconsideration and withdrawal thereof.

Applicants reiterate their comments in traverse of the application of Adachi et al. to the present claims, as set forth above.

Hanson discloses treatment of subjects for the purpose of inhibiting vaso-occlusive events, including thrombosis and embolism (abstract), i.e. blood clots. Hanson is entirely unrelated to the problem of post-surgical adhesions addressed by Adachi et al.

The Examiner cites to column 5, lines 59-60 of Hanson for the proposition that "Hanson discloses that anti-inflammatory agents inhibit adhesions". Applicants respectfully submit that the Examiner's application of Hanson is misplaced. At that point in the specification, Hanson states:

> Other useful categories of such agents include but are not limited to anti-inflammatory agents, anti-thrombotic agents, anti-platelet agents, fibrinolytic agents, lipid reducing agents, direct thrombin inhibitors, glycoprotein IIb/IIIa receptor inhibitors, agents that binds to cellular adhesion molecules and inhibit the ability of white blood cells to attach to such molecules, calcium channel blockers, beta-adrenergic receptor blockers, cyclooxygenase-2 inhibitors, and angiotensin system inhibitors. (Emphasis added).

The National Cancer Institute Dictionary of Cancer Terms (http://www.cancer.gov/Templates/db_alpha.aspx?CdrID=46480) defines cellular adhesion as "[t]he close adherence (bonding) to adjoining cell surfaces." Cellular

adhesion is clearly an intercellular phenomenon which is unrelated to post-surgical adhesions. The Examiner's attempt to relate the two distinct mechanisms based upon a reading of Hanson is at best, a leap of faith, and at worst an impermissible hindsight reconstruction of the present invention based upon a reading of the present specification.

The Examiner continues by citing to column 15, lines 66 et seq. of Hanson, wherein the patentees mention "Tranilast" as a known agent to reduce platelet count, and concludes that it would have been obvious to use Tranilast to inhibit adhesion. However, as is stated above, Hanson is directed to reducing the incidence of blood clots within veins and arteries, and not at all related to treating post-surgical adhesions, as is Adachi et al.

Accordingly, Applicants respectfully submit that Hanson is entirely misapplied in the present rejection, and represents non-analogous art as to Adachi et al. Withdrawal of the rejection is requested on this basis.

Further, even in combination, the cited references fail to disclose or suggest each and every limitation of the present claims. Neither Adachi et al. or Hanson disclose or suggest local administration of Tranilast compositions to tissues at a surgical site. Accordingly, even in combination, no *prima facie* case of obviousness can be said to exist. Withdrawal of the rejection is requested on this basis.

**Rejection under 35 U.S.C. 103 over Hubbell et al. in view of Chandrasekar et al. or Miyazawa et al. or Adachi et al. and further in view of Sheffield et al. or Hunter et al.**

Claims 1-13 are rejected under 35 U.S.C. §103(a) as obvious over Hubbell et al. in view of Chandrasekar et al. or Miyazawa et al. or Adachi et al.

and further in view of Sheffield et al. or Hunter et al. Applicants traverse this basis for rejection and respectfully request reconsideration and withdrawal thereof.

Applicants reiterate their comments in traverse of the application of Adachi et al. to the present claims, as set forth above.

Hubbell et al. disclose local delivery of fibrinolysis enhancing agents for preventing adhesions, wherein known fibrinolysis agents such as urokinase, tPA, hirudin or ancrod in a polymeric matrix are topically administered to a surgical site (abstract). As recognized by the Examiner, Hubbell et al. fail to disclose or suggest that Tranilast is a fibrinolytic agent.

Chandrasekar et al. disclose a study of the possible links between platelets and restenosis (re-growth of arterial blockage) after percutaneous transluminal coronary angioplasty (abstract) and further disclose that Tranilast and Pemirolast are effective when orally administered to rats two days prior to arterial injury, as anti-platelet-derived growth factor (PGDF) agents (page 559, left column, last paragraph; citing Miyazawa et al.).

Miyazawa et al. disclose that Tranilast and Pemirolast, both anti-allergic agents, are effective in reducing intimal thickening after endothelial injury. This study appears to be the basis upon which Chandrasekar et al. draw their conclusions as to Tranilast.

Accordingly, Chandrasekar et al. and Miyazawa et al. teach nothing more in respect to Tranilast than does Hanson, i.e. that it is effective on the intercellular level to reduce cell adhesion, which as stated above, is entirely unrelated to post-surgical adhesions.

Sheffield et al. disclose topical administration of non-steroidal anti-inflammatory drugs (NSAIDS) to the site of a surgical trauma to avoid post-surgical adhesions.

Sheffield et al. fail to disclose or suggest Tranilast as an NSAID. Notably, Applicants refer to such studies at page 3, lines 3-18 of the present specification.

Hunter et al. disclose compositions and methods for treating or preventing diseases of body passageways, particularly blood vessels, by delivering therapeutic agents to the external walls of said body passageways (col. 1, lines 14-19; col. 4, lines 48-51). Hunter et al. disclose that the therapeutic agent can be chosen from among anti-angiogenic agents, anti-proliferative agents, anti-inflammatory agents and antibiotics (col. 4, lines 26-29). In addition to these, other therapeutic agents which can be used can be selected from among those listed in columns 11-20, which include immunosuppressive agents, such as Tranilast (col. 18, line 64, bridging to col. 19, line 6).

Hunter et al. fail to disclose or suggest that any of the laundry list of therapeutic agents disclosed therein (which bridge 9 full columns of disclosure) are effective against post-surgical adhesions between tissues.

At page 12 of the outstanding Office Action, the Examiner concludes that

> Sheffield and Hunter are thus relied upon for teaching external administration of anti-inflammatory agents and anti-allergic agents such as tranilast to treat or inhibit adhesion.

Applicants respectfully submit that the Examiner's rejection is merely an untenable daisy-chain of unrelated disclosures, which obfuscates the teachings of the references themselves.

The only reference which actually suggests the efficacy of Tranilast in inhibiting post-surgical adhesions is Adachi et al., which discloses oral administration of Tranilast.

The only other references which actually address post-surgical adhesions are Hubbell et al. (which use fibrinolytic agents) and Sheffield et al. (which use NSAIDs), both of which disclose topical administration of these specific agents to post-surgical sites.

Chandrasekar et al. and Miyazawa et al. are essentially equivalent, and teach that Tranilast is a well-known anti-allergic agent (as do Hunter et al.), which may be useful in inhibiting intra-vascular restenosis after coronary artery angioplasty. Both teach oral administration. Hunter et al. is similar in that they preferably address vascular restenosis, but suggest topical administration of any of a huge laundry list of possible therapeutic agents, one of which is Tranilast, to body lumens, such as veins and arteries. Selection of Tranilast from the literally hundreds of possible therapeutic agents disclosed in Hunter et al. violates even the broadened "obvious to try" standard set forth in KSR v. Teleflex, 127 S. Ct. 1727, 1742 (2007).

None of these references disclose or suggest anything regarding the equivalence of the restenosis mechanism and the formation of post-surgical adhesions. Likewise, none of the references disclose or suggest that Tranilast would be efficacious in treating adhesions by topical or local administration.

The Examiner's conclusion, that

> Sheffield and Hunter [can be] relied upon for teaching external administration of anti-inflammatory agents and anti-allergic agents such as tranilast to treat or inhibit adhesion ... (cited above, emphasis added)

is unsupported by the teachings of the references. The Examiner's proposal amounts to an impermissible hindsight reconstruction of the present invention, based upon a reading of the present specification. It is ludicrous to suggest that one skilled in the art would look to these many, diverse and unrelated reference teachings to arrive at the presently claimed invention.

In conclusion, it is difficult, if not impossible, to imagine how one skilled in the art, in possession of these references, could conceive of the present invention absent hindsight reconstruction, which was prohibited by the Supreme Court in Diamond Rubber Co. v. Consolidated Rubber Tire Co., 220 U.S. 428 435-436 (1911).

Withdrawal of the rejection for failure to establish a *prima facie* case of obviousness is requested.

***Unexpected Results***

The Examiner is also requested to consider the data presented in the present application, which Applicants believe indicates unexpected results over the closest prior art of Adachi et al.

Applicants questioned the validity of the Adachi et al. study for various reasons (page 5, lines 14-16 and 23-26). Review of the data in Example 3 (pp. 33-34; and Tables 14 and 15 of the specification) reveals that oral administration of Tranilast is ineffective in preventing post-surgical adhesion, contrary to the suggestions of Adachi et al. The remaining examples demonstrate the efficacy of local administration of Tranilast compositions to post-surgical sites in preventing adhesions.

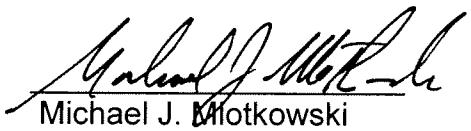
The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Account No. 50-2478 (14924).

In view of the foregoing, it is respectfully submitted that the present claims are in condition for allowance. Prompt notification of allowance is respectfully solicited.

If the Examiner has any questions or wishes to discuss this application, the Examiner is invited to contact the undersigned representative at the number set forth below.

Respectfully submitted,

Date: November 19, 2008



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